

unpatentable over Cleland et al in view of "Improving protein therapeutics with sustained release formulation" by Putney and Burke ("Putney" herein). Applicants respectfully request reconsideration in view of the following remarks.

Rejection of Claims 1-7, 13-14, 16-18 and 23-36 under 35 U.S.C. § 102(b)

Claims 1-7, 13-14, 16-18 and 23-36 are rejected under 35 U.S.C. § 102(b) as being anticipated by US Patent 5,643,605 to Cleland et al.

In order for a prior art reference to anticipate a claim, within the meaning of 35 U.S.C § 102, every limitation of the claim must be identically disclosed in that single reference.¹ The exclusion of a claimed element from the prior art reference negates anticipation.² Because the claims and every limitation thereof are neither identical nor anticipated by Cleland, et al., Applicants respectfully request that the rejections to claims 1-7, 13-14, 16-18 and 23-36 under 35 U.S.C. § 102(b) be withdrawn.

The Examiner states that:

Cleland et al. disclose methods and compositions for the encapsulation of adjuvants in PLGA microspheres (abstract). First, Cleland *et al* teach that encapsulation is a method for formulating an active agent into a composition useful for controlled release of the active agent. More specifically, Cleland *et al.* teach the PLGA is first dissolved in an organic solvent, such as methylene chloride. A concentrated antigen or adjuvant solution, or dry antigen or adjuvant is added to the polymer solution. An emulsification bath of polyvinyl alcohol is added, followed by a hardening bath to create microspheres, followed by mixing at a high speed. The microspheres can then be dried by methods such as lyophilization, vacuum drying and fluidized bed drying (c 7, l 58 – c 8, l 33).

Applicants respectfully submit that Cleland et al. does not disclose, teach or suggest all the elements of claims 1-7, 13-14, 16-18 and 23-36 as presented by the Applicants. Specifically, the cited reference discloses, teaches and suggests a method that is significantly different from, and not anticipatory of, the Applicants claimed invention. Cleland et al. teaches:

- ... the invention is a method for encapsulating adjuvant in microspheres comprising:
(a) dissolving PLGA polymer in an organic solvent to produce a solution;
(b) adding adjuvant to the solution of (a) to produce a PLGA-adjuvant mixture comprising a first emulsion;
(c) adding the mixture of step (b) to an emulsification bath to produce a microspheres comprising a second emulsion;

¹ *Corning Glass Works v. Sumitomo Electric*, 9 U.S.P.Q.2d 1962, 1965 (Fed. Cir. 1989); MPEP § 2131.

² *Connel v. Sears, Roebuck & Co.*, 220 U.S.P.Q. 193, 198 (Fed. Cir. 1983).

(d) hardening the microspheres of step (b) to produce hardened microspheres comprising encapsulated adjuvant. (Col. 3, ll. 64-67 to Col. 4, ll. 1-8; emphasis added)

In fact, Cleland, et al. teaches several critical limitations that are not required by the Applicants' invention. These critical and required limitations include (a) a two-step (double) emulsification not a one-step (single) emulsification as taught by the Applicants and (b) adds a step of "hardening" of the microspheres to "produce hardened microspheres" (see Cleland as cited above). Importantly, the absence of the above limitations would render the Cleland et al. invention inoperable. As such, claims 1-7, 13, 14, 16-18, and 23-36 are not anticipated by Cleland, et al.

Because the claims are not anticipated by Cleland et al., Applicants respectfully request that rejection of claims 1-7, 13, 14, 16-18, and 23-36 under 35 U.S.C. § 102(b) be withdrawn.

Rejection of Claims 1, 8-11, 15, and 17 under 35 U.S.C. § 103(a)

Claims 1, 8-11, 15, and 17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cleland, et al., in view of "Improving protein therapeutics with sustained release formulation" by Putney and Burke (Putney). Because the claims are not obvious in light of Cleland et al, in view of Putney, Applicants respectfully submit that claims 1, 8-11, 15, and 17 are drawn to a novel invention, not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103 for the reasons stated below.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a *prima facie* case of obviousness. In order to establish a *prima facie* case of obviousness based on one or more references, the following criteria must be met:

- (1) there must be some suggestion or motivation to modify the reference;
- (2) there must be a reasonable expectation of success; and
- (3) the reference must teach or suggest all the claim limitations. MPEP § 2143.

Moreover, the "teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure." (MPEP § 2143). Furthermore, both the invention and the prior art references must be considered as a whole. (MPEP § 2141.02).

Putney, et al. teaches “two different types of encapsulation processes that are distinguishable by the physical state, either in solution or solid, of the protein during encapsulation” (pg. 154, Col. 1, ll. 4-6). The two processes are a “double emulsion process” for “aqueous protein solutions” (pg. 154, Col. 1, paragraph 2) and an “atomization-freezing process” for “protein solids” (pg. 155, Col. 1, ll. 33-35). Together, Cleland, et al., in view of Putney both teach a “double emulsion process” for encapsulating microspheres (pg. 154, Col. 1, paragraph 2). Neither reference suggest or provide motivation to modify the two-step emulsion process to a one-step process, nor is there, by virtue of the cited reference teachings any reasonable expectation of success using anything but the double emulsion process. More importantly, the combination of cited references fails to teach at least one element of the present invention, and teaches away from the present invention by showing the necessity of a two-step emulsion process.

Therefore, it is Applicants’ position that claims 1, 8-11, 15, and 17 are not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103 for the reasons stated above. Applicants respectfully submit that the claims are in condition for allowance. Applicants respectfully request reconsideration by the Examiner, withdrawal of rejections for claims 1, 8-11, 15, and 17 and advancement of the Application to allowance.

Rejection of Claims 1 and 12 under 35 U.S.C. § 103(a)

Claims 1 and 12 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cleland et al. in view of U.S. Patent No. 5,560,438 to Collee, et al. Because the claims are not obvious in light of Cleland et al., as discussed above, Applicants respectfully submit that claims 1 and 12 are drawn to a novel invention, not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103.

Applicants respectfully request reconsideration by the Examiner, withdrawal of rejections to claims 1 and 12 and advancement of the Application to allowance.

CONCLUSION

In view of the foregoing it is respectfully submitted that pending claims 1-18 and 23-36 are drawn to novel subject matter, patentably distinct from the cited references. The

Examiner is therefore respectfully requested to reconsider and withdraw the outstanding rejections to claims 1-18 and 23-36. Accordingly, a favorable action in the form of an early Notice of Allowance is respectfully requested.

The Examiner is requested to call the undersigned for any reason that would advance the instant Application to issue. It is believed that no fee is due for this reply. If a fee is due, however, please charge this fee to our Deposit Account No. 07-0153.

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